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OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

Date: November 3, 2011

SUBJECT: Cyhalofop-butyl. Chronic Dietary Exposure Analysis to Support an Amended Tolerance for Residues in Rice and Wild Rice.

PC Code: 082583
Decision No.: 445028
Petition No.: 1F7836
Risk Assessment Type: Single Chemical/Aggregate
TXR No.: None
MRID No.: 48031201

DP Number: 395261
Registration No.: 62719-356
Regulatory Action: Section 3
Case No.: None
CAS No.: 122008-85-9
40 CFR: 180.576

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Executive Summary

A chronic aggregate dietary (food and drinking water) exposure and risk assessment was conducted using the Dietary Exposure Evaluation Model DEEM-FCID™, Version 2.03 which uses food consumption data from the U.S. Department of Agriculture's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The analysis was performed to support the establishment of an amended tolerance for wild rice and rice grain. The previous dietary assessment was completed in 2009 for wild rice and rice grain with tolerance level residues of 0.03 ppm (D358391, D. Dotson, 1/7/2009). However, crop field trials recently submitted to support a new formulation of cyhalofop have resulted in higher observed residues and created the need for amended tolerances of 0.40 ppm on wild rice and rice grain. The application rate for cyhalofop on rice and wild rice has not changed, however, so the previously generated estimated drinking water concentrations were considered appropriate for use in the current dietary exposure assessment.

Acute Dietary Exposure Results and Characterization

No toxic effects attributable to a single (i.e., acute) exposure to cyhalofop-butyl have been identified. As a result, an acute reference dose (RfD) was not established for this chemical and an acute dietary exposure assessment was not conducted.

Chronic Dietary (Food and Drinking Water) Exposure Results and Characterization

A chronic dietary (food and drinking water) exposure and risk assessment was conducted for cyhalofop-butyl using tolerance level residues, a conservative estimate of residues in drinking water, and 100% crop treated assumptions. Cyhalofop-butyl exposure associated with the amended tolerances in rice and wild rice results in an estimated risk equivalent to 5.6% of the chronic population adjusted dose (cPAD) for the U.S. population. The most highly exposed population subgroup is All Infants (<1 year old), whose risk utilizes 17.5% of the cPAD.

Cancer Dietary Exposure Results and Characterization

In accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 29, 2005), cyhalofop-butyl is classified as "not likely to be carcinogenic to humans." As a result, there is no cancer risk associated with exposure to cyhalofop-butyl.

I. Introduction

Dietary risk assessment incorporates both exposure and toxicity of a given pesticide. For acute and chronic assessments, the risk is expressed as a percentage of a maximum acceptable dose (i.e., the dose which HED has concluded will result in no unreasonable adverse health effects). This dose is referred to as the population adjusted dose (PAD). The PAD is equivalent to the point of departure (PoD, NOAEL, LOAEL, e.g.) divided by the required uncertainty or safety factors.

For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the PAD. HED is generally concerned when estimated cancer risk exceeds one in one million. References that discuss the acute and chronic risk assessments in more detail are available on the EPA/pesticides web site: "Available Information on Assessing Exposure from Pesticides, A User's Guide," 21-JUN-2000, web link: http://www.epa.gov/fedrgstr/EPA-PEST/2000/July/Day-12/6061.pdf ; or see SOP 99.6 (20-AUG-1999).

The most recent dietary risk assessment for cyhalofop-butyl was conducted by D. Dotson (Memo, D358391, 1/7/2009).

II. Residue Information

Food Residues

For cyhalofop-butyl, the residues of concern for risk assessment purposes are the combined residues of parent and its acid and diacid metabolites. Tolerances for residues of cyhalofop-butyl are established under 40CFR §180.576. Tolerances are currently established for cyhalofop-butyl and its acid and diacid metabolites in/on rice grain and wild rice at 0.03 ppm. Although rice grain is a livestock feed item, residues are not likely to occur in livestock commodities. As a result, tolerances have not been established for livestock commodities and none are included in the dietary exposure analysis. The HED-recommended amended tolerances of 0.40 ppm on rice grain and wild rice were used in this assessment. The field trial residue data for the amended tolerances have been reviewed and are adequate for supporting the petition and this dietary exposure assessment (D387444, E. Holman, November 3, 2011).

Drinking Water Residues

The estimated drinking water concentrations (EDWCs) used in the dietary risk assessment were provided by the Environmental Fate and Effects Division (EFED) in the following memorandum: "Drinking Water Assessment for the Proposed Section 3 Registration of Cyhalofop-butyl for New Uses on Wild Rice Grown in California" (D357419, K. White, 10/17/2008). The EDWC was incorporated directly into this dietary assessment into the food categories "water, direct, all sources" and "water, indirect, all sources." The use pattern remains unchanged since the 2008 EFED review and thus there are no changes in the drinking water scenarios for this amended tolerance petition.

A standard model has been developed to estimate surface water concentrations from use of pesticides on rice, the Tier I Rice Model. The model was modified to account for possible aerobic aquatic degradation and aquatic dissipation over time, and used to estimate surface water concentrations in water released from the rice paddy (tail water). Estimated drinking water concentrations (EDWCs) in groundwater were modeled using Tier I SCIGROW (version 2.3, dated July 29, 2003). EDWCs represent exposure to total residues of cyhalofop-butyl, cyhalofop-acid, and cyhalofop-diacid, with the assumption that cyhalofop-butyl and cyhalofop-acid could be present in the R or S form or as a mixture of the enantiomers. Cyhalofop-butyl and its degradates were not detected in surface water and drinking water monitoring studies conducted in California where rice is grown. The chronic groundwater and surface water

EDWCs are 0.152 and 21 ppb, respectively. As the surface water value was the higher of the two, it was used in the chronic dietary exposure analysis.

The residue values (food and drinking water) are included in Attachment 1, Chronic Residue Input File.

III. Percent Crop Treated Information

HED assumed 100 percent crop treated (PCT) for both rice and wild rice. This is considered to be a conservative assumption.

IV. DEEM-FCID™ Program and Consumption Information

The cyhalofop-butyl chronic dietary exposure assessment was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database DEEM-FCID™, Version 2.03 which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to EPA-defined food commodities (e.g. apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and EPA. For chronic exposure assessment, consumption data are averaged for the entire U.S. population and within population subgroups, but for acute exposure assessment are retained as individual consumption events. Based on analysis of the 1994-96, 98 CSFII consumption data, which took into account dietary patterns and survey respondents, HED concluded that it is most appropriate to report risk for the following population subgroups: the general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, adults 20-49, females 13-49, and adults 50+ years old.

For chronic dietary exposure assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form to produce a residue intake estimate. The resulting residue intake estimate for each food/food form is summed with the residue intake estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

V. Toxicological Information

When HED evaluated the proposed use on wild rice, the risk assessment team re-evaluated the toxicity data for cyhalofop-butyl, and updated the endpoint selection for risk assessment, as well as conclusions with respect to the FQPA Safety Factor. HED concluded the toxicity database was adequate for the purpose of risk assessment, and that the FQPA Safety Factor could be reduced to 1X. HED continues to support these findings as described in the 2009 risk assessment. HED's Cancer Assessment Review Committee evaluated mode of action data for

cyhalofop-butyl. In accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 29, 2005), the Committee classified cyhalofop-butyl as "not likely to be carcinogenic to humans" (Memo, TXR No. 0054798, J. Kidwell, 12/20/2007).

The cyhalofop-butyl dietary endpoints are summarized in Table 1, below and remain unchanged since the earlier HED assessments described above.

Table 1. Summary of Toxicological Doses and Endpoints for Cyhalofop-butyl for Use in Dietary Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	RfD/PAD	Study and Toxicological Effects
Acute Dietary (All Populations)	No appropriate endpoint attributable to a single dose was available in the current database. Therefore, an acute RfD was not established for the general U.S. population or any population subgroup.			
Chronic Dietary (All Populations)	NOAEL = 1.0 mg/kg/day	UF_A = 10x UF_H = 10x FQPA SF = 1x	Chronic RfD = 0.010 mg/kg/day Chronic PAD = 0.010 mg/kg/day	Carcinogenicity study in mice LOAEL = 10.06/10.28 mg/kg/day, M/F , based on kidney effects in females including tubular dilatation, chronic glomerulonephritis, and hyaline casts
Cancer	Classified as "not likely to be carcinogenic to humans" in accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 29, 2005).			

Point of Departure (PoD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose. RfD = reference dose.

VI. Results/Discussion

As stated above, for chronic assessments, HED is concerned when dietary risk exceeds 100% of the cPAD. The DEEM-FCID™ analyses estimate the dietary exposure of the U.S. population and various population subgroups. The results reported in Table 2 are for the general U.S. Population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50+ years. Only chronic dietary exposure has been assessed, since there is no acute endpoint, and since cyhalofop-butyl is classified as not likely to be carcinogenic.

Results of Chronic Dietary (Food and Drinking Water) Exposure Analysis

The chronic dietary exposure and risk estimates for the general U.S. population and all

population subgroups are below 100% of the cPAD. The most highly exposed subgroup is All Infants (<1 year old), whose risk utilizes 17.5% of the cPAD. The general U.S. population risk utilizes 5.6% of the cPAD. The detailed results from the chronic dietary exposure and risk assessment are summarized in Table 2, below.

Table 2. Summary of Dietary Exposure and Risk for Cyhalofop-butyl (Food and Drinking Water)

	Acute Dietary (95th Percentile)		Chronic Dietary		Cancer	
Population Subgroup*	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD	Dietary Exposure (mg/kg/day)	Risk
General U.S. Population	N/A	N/A	0.000557	5.6%	N/A	N/A
All Infants (< 1 year old)			**0.001748**	**18**		
Children 1-2 years old			0.000887	8.9		
Children 3-5 years old			0.000817	8.2		
Children 6-12 years old			0.000567	5.7		
Youth 13-19 years old			0.000426	4.3		
Adults 20-49 years old			0.000527	5.3		
Adults 50+ years old			0.000502	5.0		
Females 13-49 years old			0.000504	5.0		

VII. Characterization of Inputs/Outputs

HED conducted an unrefined dietary risk assessment for cyhalofop-butyl. The assessment assumes that all commodities with cyhalofop-butyl tolerances (i.e., rice and wild rice) contain residues of cyhalofop-butyl at the amended tolerance level. In addition, a highly conservative estimate of residues in drinking water, derived from EFED's Tier 1 rice model, was used in the assessment. Based on the conservative inputs into the analysis, it is highly unlikely that the assessment will underestimate chronic dietary exposure of the general U.S. population or any population subgroup.

Additional refinements, including the use of percent crop treated information and monitoring data for rice, as well as potential refinements in the drinking water estimates, could be incorporated into the assessment. However, as risk estimates are not of concern, a more highly refined assessment is not needed at this time.

VIII. Conclusions

A chronic dietary exposure and risk assessment was conducted to support the amended

tolerances for residues of cyhalofop-butyl in rice and wild rice. The risk estimates for the general U.S. population and all population subgroups are below HED's level of concern.

List of Attachments

1. Cyhalofop-butyl Chronic Residue Input File
2. Results of Chronic Dietary Exposure Analysis

Attachment 1: Cyhalofop-butyl Chronic Residue Input File

Filename: F:\cyhalofop\Cyhalofop 091411.R98 Chemical: Cyhalofop-butyl
RfD(Chronic): .01 mg/kg bw/day NOEL(Chronic): 1 mg/kg bw/day
RfD(Acute): 0 mg/kg bw/day NOEL(Acute): 0 mg/kg bw/day
Date created/last modified: 09-14-2011/15:36:38/8 Program ver. 2.03

EPA Code	Crop Grp	Commodity Name	Def Res (ppm)	Adj.Factors #1	#2	Comment
86010000	O	Water, direct, all sources	0.021000	1.000	1.000	
86020000	O	Water, indirect, all sources	0.021000	1.000	1.000	
15003230	15	Rice, white	0.400000	1.000	1.000	
15003231	15	Rice, white-babyfood	0.400000	1.000	1.000	
15003240	15	Rice, brown	0.400000	1.000	1.000	
15003241	15	Rice, brown-babyfood	0.400000	1.000	1.000	
15003250	15	Rice, flour	0.400000	1.000	1.000	
15003251	15	Rice, flour-babyfood	0.400000	1.000	1.000	
15003260	15	Rice, bran	0.400000	1.000	1.000	
15003261	15	Rice, bran-babyfood	0.400000	1.000	1.000	
15004050	15	Wild rice	0.400000	1.000	1.000	

Attachment 2: Results of Chronic Dietary Exposure Analysis

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U.S. Environmental Protection Agency                                    Ver. 2.00
DEEM-FCID Chronic analysis for CYHALOFOP-BUTYL                      (1994-98 data)
Residue file name: F:\cyhalofop\Cyhalofop 091411.R98
                                                Adjustment factor #2 NOT used.
Analysis Date 09-14-2011/15:37:18     Residue file dated: 09-14-2011/15:36:38/8
Reference dose (RfD, Chronic) = .01 mg/kg bw/day
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Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Population (total)	0.000557	5.6%
U.S. Population (spring season)	0.000555	5.6%
U.S. Population (summer season)	0.000594	5.9%
U.S. Population (autumn season)	0.000539	5.4%
U.S. Population (winter season)	0.000540	5.4%
Northeast region	0.000543	5.4%
Midwest region	0.000528	5.3%
Southern region	0.000514	5.1%
Western region	0.000670	6.7%
Hispanics	0.000710	7.1%
Non-hispanic whites	0.000507	5.1%
Non-hispanic blacks	0.000540	5.4%
Non-hisp/non-white/non-black	0.001070	10.7%
All infants (< 1 year)	0.001748	17.5%
Nursing infants	0.000731	7.3%
Non-nursing infants	0.002134	21.3%
Children 1-6 yrs	0.000827	8.3%
Children 7-12 yrs	0.000536	5.4%
Females 13-19 (not preg or nursing)	0.000395	3.9%
Females 20+ (not preg or nursing)	0.000520	5.2%
Females 13-50 yrs	0.000530	5.3%
Females 13+ (preg/not nursing)	0.000577	5.8%
Females 13+ (nursing)	0.000728	7.3%
Males 13-19 yrs	0.000453	4.5%
Males 20+ yrs	0.000513	5.1%
Seniors 55+	0.000497	5.0%
Children 1-2 yrs	0.000887	8.9%
Children 3-5 yrs	0.000817	8.2%
Children 6-12 yrs	0.000567	5.7%
Youth 13-19 yrs	0.000426	4.3%
Adults 20-49 yrs	0.000527	5.3%
Adults 50+ yrs	0.000502	5.0%
Females 13-49 yrs	0.000504	5.0%

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R195831

Chemical Name: Cyhalofop-butyl

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